U.S.S.N. 09/732,411
Filed: December 7, 2000
RESPONSE TO RESTRICTION REQUIREMENT

It is believed that no additional fee is required with this submission. However, should a an additional fee be required, the Commissioner is hereby authorized to charge any additional fees to Deposit Account No. 50-1868.

Remarks

Response to Restriction Requirement

In the Office Action mailed February 5, 2002, the claims were divided into forty-eight groups, Groups I-XVI, claims 1-2, 4-10, and 12-19, drawn to a method of enhancing adhesion of a target cell to a substrate comprising an amino acid SEQ ID NO:1-15 and SEV peptide; Groups XVII-XXXII, claims 1, 3, and 4-9, and 11-19, drawn to a method of inhibiting adhesion of a target cell to a substrate comprising an amino acid SEQ ID NO:1-15 and SDV peptide; and Groups XXXIII-XLVIII, claims 20-29 drawn to an adhesion modulator peptide, a substrate, a device, and a composition comprising SEQ ID NO: 1-15 and SDV peptide, and a carrier.

In response, applicants elect Group XXXI (SEQ ID NO:15), claims 1, 3, 4-9, and 11-19 with traverse.

The Examiner has asserted that in view of Table II, each SEQ ID NO. represents a structurally distinct polypeptide. However, as taught in Table II, as well as at pages 19 and 20, there is overlap regarding the types of receptor(s) and/or cells that some of the peptides bind. For example, the peptides represented by SEQ ID NO:1 and SEQ ID NO:2 exhibit a common endothelial cell attachment activity. Additionally, the peptides represented by SEQ ID NO:8 and SEQ ID NO:16, each exhibit inhibition of alpha-4 integrin binding. As disclosed at pages 19 and 20, SEQ ID NOs 14, 1, and 2, all bind to EGF like domains. Furthermore, SEQ ID NO:5 and

SEQ ID NO:10, each bind to $\alpha_v \beta_3$. The structure of each peptide is defined by the receptor to which it binds (i.e. the receptor/cell binding motif of each peptide provides the proper structure recognized by specific receptors/cell surface molecules). Accordingly, at a minimum, the number of groups that the Applicants have been restricted to should be revised based upon the receptors and cellular structures to which the claimed peptides bind. For example, SEQ ID NO.s 1, 2, and 14 are disclosed as binding to EGF-like domains and should properly belong to the same group. SEQ ID NO.s 5 and 10 each bind to $\alpha_v \beta_3$ integrins and should properly belong to the same group.

Election of Species

I. The Office Action also required election of a species from among endothelial cells, fibroblasts, macrophages, neutrophils, and myofibroblasts in Groups I-XXXII. In response, applicants elect for examination endothelial cells with traverse.

As noted in the specification, SEQ ID NO:15 (VLEP) inhibits VLA-4/VCAM interaction. VLA-4 is present on lymphocytes, monocytes, eosinophils, NK-cells, and thymocytes. VCAMs are present on, for example, cytokine activated endothelial cells. Because the VLEP peptide inhibits the VLA-4/VCAM interaction, the same peptide also inhibits cellular interaction between any of the VLA-4 harboring cells (lymphocytes, monocytes, eosinophils, NK-cells, thymocytes), and any of VCAM harboring cells (for example, endothelial cells). Cells harboring VLA-4 and/or VCAM molecules *are* target cells for SEQ ID NO:15 (VLEP). To be restricted to a species as outlined by the Examiner is improper in view of the list of target cells harboring molecules that are directly inhibited from interacting by the elected peptide above (SEQ ID

NO:15). The target cells do not exhibit mutually exclusive characteristics. Furthermore, the first paragraph on page 9 of the specification clearly demonstrates the ease in which one of skill can determine a receptor expression profile of a particular cell. Such profiles would be evident in any search for the target cell species in the prior art.

Applicants initially note that the requirement for election of species appears to be improperly drawn. The target cell species are not embodiments reciting mutually exclusive characteristics as required to make a proper election of species requirement. In this regard applicants refer to MPEP § 806.04(f) which states in relevant part:

> The general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which *under the disclosure* are found in a first species but not in a second, while a second claim recites limitations *disclosed* only for the second species and not the first. (emphasis added)

Thus, this test requires that the subject matter of claims have mutually exclusive subject matter, as disclosed in the specification, for restriction to different species. A peptide represented by SEQ ID NO:15, for example, having any of the Species of cells as a target, as outlined by the Examiner, can have inhibitory activity between any other cell harboring VCAM and any cell harboring VLA-4 molecules. Thus, a Species of a particular target cell is not mutually exclusive from any of the other species if they harbor the proper receptors/cell surface molecules for specific peptide binding.

Applicants also traverse the restriction requirement as currently set forth for the following reasons. To be valid, a restriction requirement must establish both that (1) the "inventions" are either independent or distinct, and (2) that examination of more than one of the "inventions" would constitute a burden to the Examiner. The Office Action mailed February 5, 2002, sets

forth reasons why the "species" are distinct (i.e. "structure and modes of action are different"). Applicants note, however, that election of species should not be required if the species claimed would be considered unpatentable over each other (see MPEP § 808.01(a)). Applicants urge that this point should be carefully considered by the Examiner in regard to the identified species. Notwithstanding this, applicants note that the restriction requirement does not provide sufficient basis to indicate that examination of more than one of the "species" would overly burden the Examiner. A proper search for the cell surface molecules VCAM and VLA-4, would result in cell types harboring the molecules. Alternatively, a proper search of any of the species of target cells (i.e. cells and their receptors or molecules serving as peptide binding sites) as outlined by the Examiner would uncover the various types of cell surface molecules important to the claimed peptides and their structure/function.

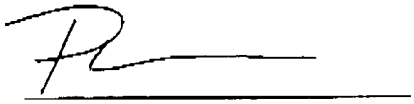
II. The Office Action also required election of a species from among a polyvinyl surface, a gel, collagen, hyaluronic acid, titanium, PGA, or others recited on page 3 of the specification in Groups I-XLVIII. In response, applicants elect for examination titanium with traverse.

The Examiner asserts that the species are distinct because their structure and modes of action are different. The "modulation of cell adhesion" refers to the modulation of cells to a substrate. The Applicants respectfully submit that the modes of action are the same for each of the species as outlined by the Examiner. Each species serves as a substrate. Although the structures of the species may be different from one another, the modes of action are the same for all (a substrate for the attachment of cells). In this case, it is not enough to restrict the Applicants

to a particular species based upon a difference in structure when the modes of action are identical.

Favorable consideration of claims 1-29 is earnestly solicited.

Respectfully submitted,



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Date: April 5, 2002

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PTO/SB/96 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S.Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Samy Ashkar

Application No./Patent No.: 09/732,411 Filed/Issue Date: December 7, 2000

Entitled: ADHESION MODULATORY PEPTIDES AND METHODS OF USE

Children's Medical Center Corporatio, a Corporation,
(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that it is:

1. [X] the assignee of the entire right, title, and interest; or

2. [ ] an assignee of less than the entire right, title and interest.
The extent (by, percentage) of its ownership interest is _____%

In the patent application/patent identified above by virtue of either:

A. [X] An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 011945 Frame 0742, or for which a copy thereof is attached.

OR

B. [ ] A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as shown below:

1. From:_____ To:_____
The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame_____, or for which a copy thereof is attached.

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3. From: Imperial College Innovations Limite To:_____
The document was recorded in the United States Patent and Trademark Office at
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[ ] Additional documents in the chain of title are listed on a supplemental sheet.

[ ] Copies of assignments or other documents in the chain of title are attached.
[NOTE: A separate copy (i.e., the original assignment document or a true copy of the original document) must be submitted to Assignment Division in accordance with 37 CFR Part 3, if the assignment is to be recorded in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

03/25/02
Date

Samy Ashkar
Typed or printed name

Signature

Principle Investigator
Title

Applicant(s): Samy Ashkar
Serial & Docket No.: 09/732,411
Filed: December 7, 2000

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8

I hereby certify that a Response to Restriction Requirement with Certificate of Transmission Via Facsimile Under 37 C.F.R. § 1.8; Fee Transmittal Sheet (in duplicate); Transmittal Form; Petition for One Month Extension of Time (in duplicate); Revocation and Power of Attorney of Entire Interest; and Statement Under 37 C.F.R. § 3.73(b); and authorization to charge/credit Deposit Account No. 50-1868 along with any paper referred to as enclosed, is being transmitted via facsimile to **TC 1600 BEFORE FINAL** at **(703) 872-9306** within the United States, to the Commissioner for Patents, Washington, D.C. 20231 on the date shown below.

Aisha Wyatt

Date: April 5, 2002

ATL1 #517950 v1

CMCC 729
078856/00032

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,411	12/07/2000	Samy Ashkar	CMZ-124CP	1508

CMZC729

959 7590 02/05/2002

LAHIVE & COCKFIELD
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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 02/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Docketed by:
By: LC
Date: 3-4-02

① 3-5-02 Rsp w/o ext
② 4-5-02 Rsp w/1 ext
③ 5-5-02 Rsp w/2 ext
④ 6-5-02 Rsp w/3 ext
⑤ 7-5-02 Rsp w/4 ext
⑥ 8-5-02 Rsp w/5 ext
Drop Dead Date

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PATENT DEPT.

RECEIVED
LAHIVE & COCKFIELD
DOCKET DEPT.
FEB - 8 2002
RETRIEVED:
FORWARDED:

PTO-90C (Rev. 07-01)

Application No.	Applicant(s)	
09/732,411	ASHKAR, SAMY	
Examiner	**Art Unit**	
Maher M. Haddad	1644	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Fax Transmission Restriction Election.

DETAILED ACTION

Sequence Compliance

1. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

Restriction Requirement

2. Please Note: In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Paula Hutzell, Ph.D., Supervisory Patent Examiner at Paula.Hutzell@uspto.gov or 703-308-4310. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

3. The following is noted:

A) Independent Claims1 and 20 include a recitation of "modulating adhesion of a target cell to a substrate" or "an adhesion modulatory peptide". Dependent claims 3, 11and 22 recite that modulating is "inhibits adhesion", whereas dependent claims 2, 10 and 21 recite that modulating is "enhances adhesion". These methods are mutually exclusive in that they reach opposing endpoints, and in that they employ structurally distinct *"piptede"* to accomplish these mutually exclusive endpoints.

Consequently, the claims have been limited to <u>either</u> a method of *inhibiting adhesion*, <u>or</u> a method of *enhancing adhesion*, irrespective of the format of the claims.

B) The specification discloses that SEQ ID NOS: 1-15 and SDV peptide each differ with respect to their structure, physiochemical properties and function (pages 9 and 10, table II). Although each peptide is proposed to be an adhesion-modulatory peptide, the specification indicates that individual peptides have different functions and widely vary in their size and composition. A person of ordinary skill in the art thus would not envision one peptide in the view of the other. Consequently, because the polypeptide of each SEQ ID NO is structurally distinct, the restriction has been set forth for each as separate groups, irrespective of the format of the claims.

4. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I-XVI. Claims 1-2, 4-10, and 12-19, drawn to a method of enhancing adhesion of a target cell to a substrate comprising an amino acid SEQ ID NO: 1-15 and SDV peptide, classified in Class 514, subclass 2.

XVII-XXXII. Claims 1, 3 and 4-9, 11-19, drawn to a method of inhibiting adhesion of a target cell to a substrate comprising an amino acid SEQ ID NO: 1-15 and SDV peptide, classified in Class 514, subclass 2.

XXXIII-XLVIII. Claims 20-29, drawn to an adhesion modulator peptide, a substrate, a device, and a composition comprising SEQ ID NO:1-15 and SDV peptide, and a carrier, classified in Class 530, subclasses 300.

5. Groups I- XXXII are different methods. A method of enhancing and a method of inhibiting adhesion differ with respect to ingredients, method steps, and endpoints; therefore, each method is patentably distinct.

6. Groups XXXIII-XLVIII. and I- XXXII are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptides of Groups XXXIII-XLVIII.can be used as an antigen for the production of antibodies, in addition to the methods of enhancing and inhibiting adhesion recited.

7. These inventions are distinct for the reasons given above. In addition, they have acquired a separate status in the art as shown by different classification and/or recognized divergent subject matter. Further, even though in some cases the classification is shared, a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Therefore restriction for examination purposes as indicated is proper.

Species Election

8. This application contains claims directed to the following patentably distinct species of the claimed Inventions I- XXXII: wherein the target cell is:

A) endothelial,
B) fibroblast,
C) macrophage,
D) neutrophil, or
E) myofibroblast.

These species are distinct because their modes of action are different.

Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

9. This application contains claims directed to the following patentably distinct species of the claimed Inventions I- XLVIII: wherein the substrate is:

A) a polyvinyl surface,
B) a gel,
C) collagen,
D) hyaluronic acid,
E) titanium,
F) PGA, or
G) others recited on page 3 of the specification.

These species are distinct because their structure and modes of action are different.

Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

10. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. M.P.E.P. § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

11. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (703) 306-3472. The examiner can normally be reached Monday through Friday from 8:00 AM to 4:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
February 1, 2002

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
2/4/02